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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/823,365	PASTERNAK ET AL.	
	Examiner	Art Unit	
	KARA R. MCMILLIAN	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,16-20 and 22-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *11,16-20 and 22-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 3, 2008 has been entered.

Response to Amendments/Arguments

No amendments were made to the claims. Claims 1-10, 12-15 and 21 are canceled. Claims 11, 16-20 and 22-35 are pending.

Applicant's arguments filed November 3, 2008 have been fully considered but they are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants argue that taken alone or in any combination, the prior art references of the prior rejection under 35 USC 103 over Saito et al. in view of Goodman and

Gilman, Elkhoury et al. and Ptchelintsev et al. do not teach applicants claimed invention. Applicants disagree with the examiners conclusions that it would have been logical to combine the teachings of the recited references given that the analgesic properties were each known individually in the art and their synergistic effect would have been expected.

Applicants argue that topical combination of morphine and butamben in the periphery produces a synergistic result that would have been unexpected since prior to the teachings of the instant application, peripheral mechanisms in the mediation of antinociceptive responses were unknown. Applicants further argue that opioid analgesia was largely perceived to be mediated through the central nervous system (systemically) and not through opioid receptors located at peripheral sites and that those skilled in the art did not appreciate the significance of opioid stimulation at peripheral sites, much less the significance of combining opioid analgesics and local anesthetic at these peripheral sites. Applicants also provide several references teaching that the topical use of morphine fail to stimulate peripheral sites.

These arguments are found not persuasive since Elkhoury et al. teach that opioid analgesia is mediated through opioid receptors located at peripheral sites. Elkhoury et al. teach the topical application of opioid analgesic drugs such as morphine in diluted solutions to produce an analgesic effect in a localized area and without a transdermal migration of the opioid drug into the blood stream (see abstract). Elkhoury et al. further teach that even prior to said invention it was discovered that opioid receptors are also located in other peripheral tissues and that antinociceptive effects of mu- and kappa-

agonists in inflammation are enhanced by a peripheral opioid receptor-specific mechanism of action (see column 2 lines 3-26). Elkhoury et al. further teach that a large number of animal studies were performed to characterize peripheral opioid receptors and their activation by morphine and other opioid drugs and that a most important determination from these studies revealed that the doses of drugs required to produce analgesia in the peripheral tissues were extremely small and therefore devoid of side effects produced by dosages sufficient to operate on the brain (see column 2 lines 12-26). Thus Elkhoury et al. teach that peripheral analgesia of morphine was known at the time of the instant invention.

Applicants further argue that the synergistic effect in the peripheral of the combination of morphine and butamben was unexpected and that the teachings of Saito et al. only teach the synergistic effect systemically which does not predict the outcome of topical application. Applicants further submit a declaration by Sandra C. Roerig filed on August 16, 2007 providing evidence of the state of the art at the time of the instant invention. The declaration states that topical administration of morphine and lidocaine produced an unexpected synergistic antinociceptive response in the periphery and that studies of this kind had never been performed.

These arguments are found not persuasive since the recited prior art references teach that both butamben and morphine are known local analgesics which act in the periphery. Therefore it would be obvious to combine two drugs useful for the same purpose in order to achieve an increased effect. "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same

purpose, in order to form a third composition to be used for the very same purpose .... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850,205 USPQ 1069, 1072 (CCPA 1980).

Furthermore, Saito et al. teach that morphine combined with a similar local anesthetic (lidocaine) with the same mechanism of action as butamben, produce synergistic effects systemically. One of ordinary skill in the art would reasonably expect that the combination would also produce synergism when combined in the periphery since butamben is a known local anesthetic with action in the periphery that is applied topically and morphine induces analgesia either systemically or peripherally by binding to opioid receptors in the brain or in peripheral tissues to induce analgesia and since butamben and morphine have different mechanisms of action from each other. Furthermore, the declaration filed on May 1, 2006 by Yuri Kolesnikov and Gavril Pasternak, introduces the journal article Kolesnikov et al. (Anesth Analg, 2003 Volume 97, pages 1103-1107) which describe the data showing analgesic synergy between local administration of morphine and butamben. Kolesnikov et al. conclude that the synergistic effects of topical lidocaine and morphine were not unexpected and that synergistic interactions are more likely when drugs act on different mechanisms, as shown between morphine and butamben (see page 1107). Thus there is a reasonable expectation of success that when butamben is administered topically with morphine, a synergistic effect would occur and therefore the synergistic results as claimed in the instant application is not unexpected.

Furthermore Applicants data with regard to synergism between topical administration of butamben and morphine are not commensurate in scope with Applicants claimed invention. Claim 11 of the instant application claim synergistically effective amounts of morphine and butamben without providing specific doses of each drug. Claims 16-20 and 22-26 claim wide ranges of morphine and butamben concentrations. However, the data provided by Applicants in the declaration filed on May 1, 2006 show that the administration of morphine and butamben applied locally produce a synergistic effect when the combination is applied at a fixed ratio of 1:0.4 of morphine to butamben.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the applicants have argued that although Elkhoury et al. and Ptchelintsev et al. teach the topical anesthetic properties of each of morphine and butamben, there is no expectation of their synergistic effect in the periphery, and Saito et al. do not rectify this deficiency as the synergistic effect described systemically by Saito et al. would not be anticipated when administered topically. The examiner respectfully points out again that synergy was expected due to the many references (presented by applicant as prior art) including

Saito et al. described above and as detailed below in the art rejection demonstrating synergy between morphine/lidocaine and morphine/bupivacaine. As lidocaine, bupivacaine and butamben all posses the same mechanism of action and as lidocaine and bupivacaine have demonstrable synergy with morphine it would be reasonable to one of ordinary skill in the art that other local anesthetics acting through the same mechanism of action would posses similar synergy with morphine whether applied systemically or locally. Thus though synergy has been demonstrated by the applicants, it is not an unexpected result.

Claims 27-32 were rejected under 35 USC 103 as described above and further in view of Mayer et al. Claims 34-35 were also rejected under 35 USC 103 as describe above and further in view of Soo et al. Applicants only argue that the combination of Mayer et al. or Soo et al. do not remedy the deficiencies of Saito et al. in view of Goodman and Gilman, Elkhoury et al. and Ptchelintsev et al. This argument is found not persuasive as discussed above.

For the reasons set forth above and for the reasons of record the prior rejections under 35 USC 103 are maintained, however, a modified rejection is presented below for better clarification.

This action is made **non-final**.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11, 16-20, 22-26 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elkhoury et al. U.S. Patent No. 5,589,480 (provided on IDS) in view of Elden U.S. Patent No. 5,814,659 and further in view Saito et al. (1998, Anesthesiology, Volume 89(6), pages 1455-1463-provided on IDS) and Goodman and Gilman (The Pharmacological Basis of Therapeutics, seventh edition, pages 302-305 and 310-312).

Claims 11, 16-20, 22-26 and 33 of the instant application claim a method of providing topical analgesia comprising administering to peripheral sites synergistically effective amount of morphine and butamben.

Elkhoury et al. teach the topical administration of an opioid drug, such as morphine, to produce an analgesic effect in a localized peripheral area and without a transdermal migration of the opioid drug into the blood stream (see Abstract). Elkhoury et al. further teach that it has been determined in the present invention that extremely small systemically inactive doses of both conventional opioid drugs such as morphine and other opioids can produce potent analgesic effects after local application in peripheral tissue (see column 2, lines 55-60). Elkhoury et al. further teach that the opioid may be applied using a variety of different topical formulations such as sprays, gels, creams, etc. and can be applied to the skin to relieve pain without the typical side effects associated with oral or injectable narcotics (see column 4, lines 46-57). Elkhoury et al. teach in column 5 lines 5-13 a specific example of a morphine spray wherein 90 mg of morphine is provided in a total of 129 ml of saline solution which is equivalent to approximately 0.07% of morphine provided in the solution.

Elkhoury et al. do not teach the inclusion of butamben and thus a synergistic combination.

Elden teaches topical analgesic compositions and methods for inducing topical analgesia (see abstract). Elden teaches compositions comprising an analgesic agent such as butamben picrate (see column 2 lines 14-18). Elden further teaches that the method of providing topical analgesia comprises bringing the topical analgesic

composition (for example applied to a cotton strip or inserted into a typical skin-wipe packet) in contact with the skin of a person in need of such analgesia and maintaining the composition in contact with the skin for a period of time sufficient to induce and maintain topical analgesia (see column 3 lines 3-11). Elden further teaches a number of topical agents are known in the art such as butamben picrate and that the analgesic agent typically comprises from about 0.2 to 20 % by weight of the final composition (column 3 lines 27-34). Furthermore, claims 1-2 of Elden claim a topical analgesic composition comprising from about 0.2 to about 20 weight percent of an agent selected from benzocaine, butamben picrate, lidocaine, etc.

Accordingly, one of ordinary skill in the art at the time of the instant invention would have found it obvious to combine the teachings of Elkhoury et al., which teach topical analgesic compositions comprising morphine and other opioids for the treatment of pain, with the teachings of Elden, which teach topical analgesic compositions comprising butamben for the relief of pain. Thus, since both morphine and butamben are both topical analgesics useful for local administration for the relief of pain, one of ordinary skill in the art would be motivated to combine morphine and butamben in a composition with a reasonable expectation of success in providing an improved treatment of localized pain upon local administration of the composition. "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose ....[T]he idea of combining them flows logically from their having been

individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850,205 USPQ 1069, 1072 (CCPA 1980).

One of ordinary skill in the art would also be motivated to combine the morphine and butamben in a composition based on the concentrations taught in the prior art references (0.07% of morphine (Elkhoury et al.) and between 0.2%-20% of butamben (Elden)). Elkhoury et al. and Elden teach overlapping ranges of concentrations of morphine and butamben as claimed in claims 16, 17, 19, 20 and 22-25 of the instant application. Thus since the composition of morphine and butamben is rendered obvious it would also be obvious to one of ordinary skill in the art that the combination would produce a synergistic effect since it is obvious to combine the compounds in similar concentrations as claimed in the instant application (as taught by Elkhoury et al. and Elden). A compound and its properties are inseparable. In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963).

Elkhoury et al. and Elden do not teach concentrations of morphine as claimed in claim 18 of the instant application and concentrations of butamben as claimed in claim 26 of the instant application. However, it would be within the skill of an ordinary skilled artisan to modify the concentrations of the drugs within the composition based upon the effect desired. It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See In re Boesch, 205 USPQ 215 (CCPA 1980). Furthermore, it is obvious to vary and/or optimize the amount of a compound provided in the composition, to provide a composition having the desired properties such as the desired (ratios,

concentrations, percentages, etc.). It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Furthermore the teachings of Saito et al. in view of Goodman and Gilman render obvious the synergistic combination of morphine and butamben. Saito et al. teach, on page 9, that morphine and lidocaine have a synergistic antinociceptive interaction in both bolus injections and in continuous coinfusion in which the agents are administered in small volumes and low concentrations. Further Saito et al. notes that in a recent study it was shown that morphine and bupivacaine induced a faster onset and a modest hypoalgesic effect than when administered separately. On page 10, Saito et al., teach that different opioid receptor subtypes have different characteristics and demonstrate different antinociceptive effects; further individual local anesthetics have different features, such as potency, duration, and motor block. Thus different opioid sub-types can have differing mechanisms of action, whereas the local anesthetics (like lidocaine and bupivacaine) have the same mechanism of action but differ in their pharmacological properties.

Goodman and Gilman teach, on pages 302-303 that local anesthetics have many actions in common and their primary mechanism of action involves a block of conduction by decreasing the large transient increase in the permeability of the membrane to sodium ions that is produced by a slight depolarization of the membrane. On page 310 the pharmacological action of lidocaine and procaine are as previously

detailed (see above mechanism of action). On page 312 Goodman and Gilman detail two local anesthetics with low aqueous solubility, namely benzocaine (structurally identical to procaine without the terminal diethylamino group) and butamben picrate. It is taught that these compounds can be applied directly to wounds and ulcerated surfaces as their poor solubility makes their systemic absorption too slow to be toxic. Further when applied they remain localized for long periods of time to produce a sustained anesthetic action.

It would have been obvious to one of ordinary skill in the art that the combination of butamben and morphine would result in a synergistic effect since Saito et al. teach that it is known that administration of morphine with lidocaine results in a synergistic antinociceptive effect and Goodman and Gilman demonstrate that local anesthetics such as lidocaine and butamben have the same mechanism of action (sodium ion effect). One of ordinary skill in the art would have expected that butamben would posses synergistic activity with morphine as butamben's mechanism of action is the same as lidocaine and further as Saito et al. point out that synergistic activity has been seen with another local anesthetic (bupivacaine) in conjunction with morphine. Although Saito et al. teaches synergistic effects upon systemic administration, an ordinary skilled artisan would also expect the same synergistic effect when administered peripherally since the combination is able to produce a synergistic effect systemically and it is known that morphine induces analgesia either systemically or peripherally by binding to opioid receptors in the brain or in peripheral tissues to induce analgesia. Furthermore, since butamben and morphine have different mechanisms of action from

each other it is likely that the combination would be greater than additive and likely synergistic.

Claims 27-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elkhoury et al. U.S. Patent No. 5,589,480 (provided on IDS) in view of Elden U.S. Patent No. 5,814,659 and further in view Saito et al. (1998, Anesthesiology, Volume 89(6), pages 1455-1463-provided on IDS) and Goodman and Gilman (The Pharmacological Basis of Therapeutics, seventh edition, pages 302-305 and 310-312) as applied to claims 11, 16-20, 22-26 and 33 above, and further in view of Mayer et al. U.S. Patent No. 5,840,731.

Elkhoury et al. in view of Elden and further in view Saito et al. and Goodman and Gilman is as set forth above

The recited references lack a teaching of an NMDA receptor antagonist.

Mayer et al. teach that the analgesic effectiveness of a combination drug composition comprising at least one analgesic is significantly enhanced by the addition of an NMDA receptor antagonist (see Abstract). Mayer et al. teach compositions comprising a first analgesic, a second component, and an analgesia-enhancing amount of an NMDA receptor antagonist and methods of treatment for alleviating pain by the administration thereof (column 1, lines 6-27; column 2, lines 30 to column 3, line 5; column 4, line 67 to column 5, line 13). Analgesics are taught to be selected from morphine, fentanyl, etc. (column 3, lines 57-65). NMDA receptor antagonists are taught to be selected from dextromethorphan, dextrophan, ketamine, memantine,

pyrroloquinoline quinone, and cis-4-(phosphonomethyl)-2-piperidinecarboxlic acid (column 4, lines 33-50). Further, claims 1 and 2 of Mayer et al. claim methods and compositions for alleviating pain comprising a composition comprising an analgesic (e.g. morphine), a non-opioid analgesic, and a nontoxic NMDA receptor antagonist (e.g. dextromethorphan).

Mayer et al. further teach the amount of the nontoxic NMDA receptor antagonist will be at least that which is required to significantly enhance the analgesic effectiveness of the analgesics present in the dose and that suitable amounts of the antagonist can readily be determined by employing routine procedures (see column 4 lines 55-61). Generally the amounts of the antagonists can vary from about 10 to about 100 and preferably from about 15 to about 60 mg per unit dose (see column 4 lines 61-65). Examples 1-26 in columns 6 and 7 teach specific examples of compositions comprising 30 mg of dextromethorphan as the NMDA receptor antagonist which is approximately 4% or more of the total composition.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to administer a topical composition comprising the morphine, butamben and an NMDA receptor antagonist because (1) Elkhoury et al. and Elden teach the morphine and butamben, respectively, as analgesics suitable for topical administration; and (2) Mayer et al. teach that the addition of an NMDA receptor antagonist (e.g. ketamine) to an analgesic composition is known in the art to significantly enhance the analgesia provided thereby. One of ordinary skill in the art would have been motivated to prepare and utilize such a composition because of an

expectation of success in providing a topical composition suitable for peripheral relief with significantly enhanced analgesic effects, as taught by Mayer et al.

It is noted that Mayer et al. teach the NMDA receptor antagonists disclosed therein for achieving improved analgesia generally. Mayer et al. specifically teach amounts of NMDA receptor antagonists of about 4% or greater. Although Mayer et al. does not specifically teach lower concentrations as claimed in claims 31 and 32 of the instant application, Mayer et al. teach that the amount of the nontoxic NMDA receptor antagonist will be at least that which is required to significantly enhance the analgesic effectiveness of the analgesics present in the dose and that suitable amounts of the antagonist can readily be determined by employing routine procedures. Accordingly, it has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See In re Boesch, 205 USPQ 215 (CCPA 1980). Furthermore, it is obvious to vary and/or optimize the amount of a compound provided in the composition, to provide a composition having the desired properties such as the desired (ratios, concentrations, percentages, etc.). It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Claims 34-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elkhoury et al. U.S. Patent No. 5,589,480 (provided on IDS) in view of Elden U.S.

Patent No. 5,814,659 and further in view Saito et al. (1998, Anesthesiology, Volume 89(6), pages 1455-1463-provided on IDS) and Goodman and Gilman (The Pharmacological Basis of Therapeutics, seventh edition, pages 302-305 and 310-312) as applied to claims 11, 16-20, 22-26 and 33 above, and further in view of Soo U.S. Patent No. 5,028,595.

Elkhoury et al. in view of Elden and further in view Saito et al. and Goodman and Gilman is as set forth above. Furthermore, it is noted that Elkhoury et al. specifically teach the treatment of painful conditions associated with inflammation (column 2, lines 51-60).

The recited prior art references do not specifically disclose the treatment of acute and chronic peripheral neuropathy and neuropathic inflammation.

Soo teaches that morphine is known in the art for the treatment of peripheral neuropathy (column 1 lines 62-66).

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat the claimed conditions because (1) Elkhoury et al. teaches that morphine is known in the art to treat painful inflammatory disorders in general; and (2) Soo teaches that morphine is known in the art to treat peripheral neuropathy. One would have been motivated to treat the claimed conditions with the morphine compositions of the invention because of an expectation of success in treating the pain associated with the conditions.

Conclusions

Claims 1-10, 12-15, and 21 are canceled. Claims 11, 16-20, and 22-35 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARA R. MCMILLIAN whose telephone number is (571)270-5236. The examiner can normally be reached on Monday-Thursday from 8:30 am- 6:00 pm and every other Friday from 8:30 am- 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kara R. McMillian/
Examiner, Art Unit 1617

KRM

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617